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Estimating Latent Attitudinal and Behavioral Risk Profiles and Associations with Food Allergy-Related Quality of Life

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OBJECTIVES/GOALS: Childhood food allergy (FA) is a chronic condition that can profoundly impact patient and caregiver quality of life (QoL). Risk factors for impaired FA-related QoL remain largely unknown. This study aims to estimate latent profiles of caregiver attitudes and behaviors, and examine if group membership correlates with established QoL outcomes. **METHODS/STUDY POPULATION:** This project is subsumed under the FORWARD study (5R01AI130348-04), a multisite longitudinal cohort study conducted at four major pediatric medical centers. Eligible participants include caregivers of children ages 12 years and under who identify as Black or White and have at least one physician-diagnosed FA. Participants complete intake surveys, annual clinical visits, and quarterly surveys administered via REDCap. As of November 2022, 413 Non-Hispanic Black and 486 Non-Hispanic White participants were enrolled. **RESULTS/ANTICIPATED RESULTS:** We anticipate that specific latent profiles will emerge based on caregiver-reported attitudes and behaviors. We predict these profiles will demonstrate configural, metric, and scalar invariance across key sociodemographic strata (e.g., child race/ethnicity, household income, caregiver educational attainment, and child sex). Relatedly, we anticipate that sociodemographic factors, such as race, sex, ethnicity, parental education, and income, will significantly predict group membership. Finally, we predict that latent profile membership will be associated with different levels of quality of life, as assessed by the parental food allergy-related quality of life questionnaire (FAQLQ-PF-10) and other validated measures of FA-related psychosocial burden. **DISCUSSION/SIGNIFICANCE:** Given the psychosocial burden associated with FA, and limited mental health resources for patients and families, it is essential to improve understanding of how caregiver attitudes influence behavior and disease management outcomes. In so doing, we will inform the development and implementation of tailored interventions for those at highest risk.

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Fc gamma receptor crosslinking promotes antibody-induced LILRB4 internalization and immune regulation of acute monocytic leukemia

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OBJECTIVES/GOALS: The aims of this study were to: 1) determine the involvement of each Fc gamma receptor isoform in antibody-mediated crosslinking and internalization of LILRB4 in acute monocytic leukemia and 2) elucidate the role of this crosslinking and internalization in antibody-mediated immune regulation of these malignant cells. **METHODS/STUDY POPULATION:** To determine the involvement of Fc gamma receptors in antibody-mediated complex internalization, we generated acute monocytic leukemia cell lines with CRISPR-Cas9 knockout of each Fc gamma receptor isoform. We tested the effects of each knockout on anti-LILRB4 antibody-mediated internalization by flow

cytometry and confirmed our findings with confocal microscopy. To elucidate the role of this crosslinking and internalization in immune regulation of acute monocytic leukemia, we conducted preliminary ELISA-based studies of the inflammatory signaling and cytokine release profiles of wild-type and Fc gamma receptor knockout cells treated with the LILRB4-targeting antibody. **RESULTS/ANTICIPATED RESULTS:** We have concluded that Fc gamma receptor I (CD64) plays a role in LILRB4 crosslinking and internalization by our anti-LILRB4 antibody and there are also contributions from Fc gamma receptor IIA (CD32A) observed in the absence of CD64 on the cell surface. Preliminary signaling studies have demonstrated that Fc gamma receptor-mediated antibody crosslinking and internalization of LILRB4 decreases anti-inflammatory signaling downstream of Fc gamma receptors, particularly in the absence of CD64 on the cell surface. The immunomodulatory effect of antibody-mediated LILRB4 crosslinking and internalization is being confirmed in follow-up signaling, cytokine release and lymphocyte activation studies. **DISCUSSION/SIGNIFICANCE:** This study will improve the efficacy of LILRB4-targeting antibody therapeutics for patients suffering from acute monocytic leukemia and help characterize CD64 and CD32A as potential clinical biomarkers for patients undergoing LILRB4-targeting antibody immunotherapeutic treatment, currently in first-in-human clinical trials.

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Food Intake Restriction for Health Outcome Support and Education (FIREHOUSE): a Proof of Concept Randomized Clinical Trial

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OBJECTIVES/GOALS: Particulate matter (PM) and metabolic syndrome (MetSyn) increase risk of World Trade Center-Lung Injury (WTC-LI). Mediterranean-type diets have also been found to improve lung function. Fire Department of New York 1st-responders with a high PM exposure at WTC and MetSyn may have improved lung function after a Mediterranean dietary intervention. **METHODS/STUDY POPULATION:** Food Intake REstriction for Health OUtcome Support and Education (FIREHOUSE) randomized clinical trial (RCT) assessed our hypothesis that a low-calorie Mediterranean (LoCalMed) intervention targeting clinically relevant disease modifiers will improve metabolic risk, subclinical indicators of cardiopulmonary disease, quality of life, and lung function in firefighters with WTC-LI. Primary-outcome targeted a LoCalMed loss of BMI ($\geq 1\text{kg/m}^2$). Secondary-outcomes included lung function, quality of life, and cardiovascular health. Male firefighters with WTC-LI and a BMI $> 27\text{kg/m}^2$ were randomized to: 1. LoCalMed (n=46); or 2. Usual Care (UC; n=43). Clinicaltrials.gov:NCT03581006. **RESULTS/ANTICIPATED RESULTS:** LoCalMed's estimated efficacy on BMI reduction crossed the pre-specified significance boundary on interim analysis compared to UC. In addition, improvements were observed in secondary-outcomes of lung health (FEV1 and FVC), inflammation (WBC), vascular disease (DBP), quality of life (SF-36, health perception) and dietary habits (less cholesterol, carbohydrates, fats, and sweets and increased protein) in the LoCalMed arm. **DISCUSSION/SIGNIFICANCE:** LoCalMed significantly decreased BMI and alleviated adverse health outcomes in our WTC-exposed first responders. A fully powered RCT is required to determine if this approach is efficacious for the treatment of WTC-associated pulmonary disease, as well as LoCalMed's generalizability to PM associated disease.